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OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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Subject: **Agency Comments on Bayer CropScience Draft Study Protocol (submitted 4/6/2016) for the Colony Feeding Study Evaluating the Chronic Effects of Clothianidin-Fortified Sugar Diet on Honey Bee Colony Performance Under Free Foraging Conditions.**

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DRAFT

The Environmental Fate and Effects Division (EFED), in conjunction with Canada's Pesticide Management Regulatory Agency (PMRA) and the California Department of Pesticide Regulation (CDPR), have reviewed a test protocol for clothianidin entitled, "Colony feeding study evaluating the chronic effects of clothianidin-fortified sugar diet on honey bee (*Apis mellifera*) colony performance under free foraging conditions." The protocol was submitted by Bayer CropScience (BCS) as part of the Registration Review Data Call-In requirements for clothianidin to address issues posed by the lack of overwintering success in the previous colony feeding study (MRID

49836101). This document details the Agencies response to this revised protocol. The Agencies had previously indicated (at the March 2, 2016 meeting between the registrants and EPA) that certain changes to the protocol should be made in order to improve the potential for control hives to successfully overwinter without needing Agency approval. A final protocol does not need to be submitted independently, but should be submitted as an appendix to the final study report.

General Comment:

During the study it is expected that test bees will be managed according to local best management practices and therefore the Agencies do not necessarily need to be consulted, for instance, when hives are treated for *Varroa*, provided with supplemental feed or need to be moved to protect weak hives. The Agencies would still like to be updated as decisions are made including a rationale behind the management decision. The Agencies are open to consult with the registrant whenever a decision is to be made that is not in keeping with local best management practices.

1. Concentrations for colony feeding study.

Registrant proposals:

The previous study (MRID 49836101) used nominal test concentrations of 10, 20, 40, 80 and 160 µg/L. The proposed nominal test concentrations indicated in the protocol are for 10, 20, 30, 40, and 80. The registrant indicated that in the previous study, clear effects occurred at both the 80 and 160 µg/L treatment groups and therefore the addition of the 30 µg/L treatment group in the new study adds more value than continuing with both the 80 and 160 µg/L treatment groups.

Agency Response:

The Agencies are concerned that given the inherent variability of the test system, that the narrow dose progression of the proposed dose spacing may actually be a confounding factor for study interpretation, making it difficult to ascertain a dose-response. Therefore, the Agencies do not support the proposal to add an additional dose between 20 and 40 µg/L. The Agencies recommend maintaining consistency in treatments for 0, 10, 20, 40, and 80 µg/L levels. The Agencies anticipate comparing the 2015 and 2017 study data to measure the stability of dose related effects over years. Additionally, a high dose is desirable to pin the effects for death of hives as noted in the 2015 study at 160 ppb. One alternative might be to lower the highest dose (*e.g.* 100 or 120 µg/L).

2. Feeding Timing

The previous study provided colonies with 2.4 L of spiked syrup per week during the exposure period. Given that control colonies consumed nearly all (93—100%) of the sugar syrup during this period, the Agencies agree that colonies should be fed some additional syrup. However, the Agencies would appreciate if the registrant could provide justification for feeding 4 liters of sugar solution per week, possibly putting this value in context of the colony's bioenergetics during the exposure phase. Alternately, if time allows, the appropriate amount of treated sucrose required to feed the colony could be determined based on the number of bees recorded from the 2rd CCA, just prior to exposure initiation.

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3. Regarding CCA assessments for colony strength using digital photography.

BCS has indicated on page 9 of the revised clothianidin protocol that assessments will be made by visual assessments. The same page also indicates that digital photography of the frames will be performed, but it was unclear to the Agencies whether this was only for the calibration exercise, or if digital photography will be used during some of the CCAs as well. This should be clarified in the final protocol. As noted for the previous protocol review (D420684), the same method should be used consistently throughout the study.

4. Varroa and Nosema Testing/Treatment

The Agencies have indicated that post-exposure treatments can be conducted for Varroa or Nosema, without prior consultation and the protocol indicates that testing for Varroa and Nosema will occur at the 2nd (pre-exposure), 4th (immediately following exposure) and 8th CCAs (final CCA in April, 2017). However, the Agencies recommend that any post-exposure treatments of Varroa/Nosema do not occur until after one brood cycle has been completed following exposure (*i.e.* 3 weeks following CCA 4) to elucidate if there are any combined treatment/pathogen effects. Additionally, to gain a better understanding of the overall pest/pathogen incidence of hives immediately before overwintering, the Agencies request that an additional sampling period for *Varroa* and *Nosema* take place during CCA6 unless it is deemed a health risk to the colony. Determination of pathogen treatments should be based on the condition of control hives or local best management practices for beekeeping. If treatment is deemed necessary, it should be conducted on all control and treatment hives.

5. Residue sampling of Hive Matrices

The revised protocol specifies that uncapped nectar, capped honey and pollen stores will be collected from subsamples from a minimum of three different frame sides. The Agencies are concerned that this may still not provide a representative sampling of in-hive exposure as residues are unlikely to be distributed homogenously throughout the hive matrices. Therefore, the Agencies propose that each hive matrix is sampled from at least one location on five frames per hive (however, both sides of a frame need not be sampled). The Agencies also request that bee bread be additionally sampled at CCA 6 (in addition to the sampling at CCAs 2 and 4, which are currently listed in the protocol's chronology list table.

6. Additional recommendations:

We recommend marking the queen for each hive. Marking the queen at each CCA will allow for tracking the queen (e.g. indicate if the queen has been replaced) and allow for quantification of the extent of supersedure. In the event of a lost queen, the queen should not be replaced. Only normal supercedure should replace a queen. If normal supercedure occurs, the event should be documented and the new queen marked.

The final protocol should also include the criteria for the addition and removal of supers and the final report should include further details regarding their placement (*e.g.* dates, whether frames/bees are redistributed between hive bodies after super addition/removal, etc.).

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